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**Dalko et al.**(10) **Patent No.:** **US 9,421,157 B2**  
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None

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(56) **References Cited****U.S. PATENT DOCUMENTS**3,915,300 A 10/1975 Gatley  
4,234,435 A 11/1980 Meinhardt et al.  
4,252,951 A 2/1981 Jackson et al.  
4,446,312 A 5/1984 Noyori et al.  
4,509,949 A 4/1985 Huang et al.  
4,708,753 A 11/1987 Forsberg  
4,919,179 A 4/1990 Chattopadhyay  
4,931,110 A 6/1990 McKenzie et al.  
4,983,382 A 1/1991 Wilmott et al.  
5,089,578 A 2/1992 Valint et al.5,129,972 A 7/1992 Riga et al.  
5,346,693 A 9/1994 Pilleux  
5,412,004 A 5/1995 Tachibana et al.  
5,492,426 A 2/1996 Gueret  
5,518,517 A 5/1996 Jahnke et al.  
5,607,921 A 3/1997 Bernard et al.  
5,789,385 A 8/1998 Anderson et al.  
5,811,487 A 9/1998 Schulz, Jr. et al.  
5,858,055 A 1/1999 Jahnke et al.  
6,099,870 A 8/2000 Cauwenbergh  
6,194,452 B1 2/2001 Murad  
6,306,376 B1 10/2001 Philippe  
6,328,495 B1 12/2001 Gueret  
6,413,936 B1 7/2002 Schmidt et al.  
6,484,731 B1 11/2002 Lacout  
6,495,147 B1 12/2002 Dumas et al.  
6,645,476 B1 11/2003 Morschhäuser et al.  
6,987,128 B2 1/2006 Dalko et al.  
7,049,300 B2 \* 5/2006 Dalko et al. .... 514/23  
7,079,300 B1 \* 7/2006 Govyadinov et al. .... 359/288  
7,153,498 B2 12/2006 Aubrun-Sonneville et al.  
7,666,847 B2 2/2010 Houllmont et al.  
7,732,414 B2 \* 6/2010 Dalko et al. .... 514/23  
8,088,399 B2 \* 1/2012 De Lacharriere et al. .... 424/401  
2003/0044439 A1 3/2003 Dobson, Jr. et al.  
2003/0124079 A1 7/2003 Mougin et al.  
2003/0147830 A1 \* 8/2003 Phillips et al. .... 424/70.14  
2003/0152600 A1 8/2003 Dalko et al.  
2004/0005342 A1 1/2004 Bernerd  
2004/0048785 A1 3/2004 Dalko et al.  
2004/0234464 A1 11/2004 Herve  
2005/0002889 A1 \* 1/2005 Dalko et al. .... 424/70.13  
2005/0250708 A1 11/2005 Trouille  
2006/0223763 A1 10/2006 Dalko et al.  
2008/0003191 A1 1/2008 Simonnet et al.  
2008/0008674 A1 1/2008 Burnier et al.  
2008/0014162 A1 \* 1/2008 Willemin et al. .... 424/70.1  
2008/0014230 A1 \* 1/2008 Pineau et al. .... 424/401  
2008/0026020 A1 1/2008 Willemin et al.  
2008/0226756 A1 \* 9/2008 Willemin et al. .... 424/732  
2009/0041691 A1 \* 2/2009 Candau et al. .... 424/60  
2009/0075935 A1 \* 3/2009 Bissey et al. .... 514/54  
2009/0274638 A1 \* 11/2009 Pineau et al. .... 424/59  
2010/0168055 A1 \* 7/2010 Laboureau et al. .... 514/53  
2010/0190742 A1 \* 7/2010 Breton et al. .... 514/54**FOREIGN PATENT DOCUMENTS**DE 27 03 185 A1 8/1978  
EP 0 173 109 A2 3/1986

(Continued)

**OTHER PUBLICATIONS**

Jordan, Tamoxifen: A Most Unlikely Pioneering Medicine, Nature Review: Drug Discovery, vol. 2, Mar. 2003, p. 205.\*

(Continued)

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(57) **ABSTRACT**

A cosmetic use of at least one C-glycoside derivative in a composition comprising a physiologically acceptable medium, as a cosmetic agent for promoting the desquamation of the skin and/or the scalp and/or for stimulating epidermal renewal.

**9 Claims, No Drawings**

(56)

## References Cited

## FOREIGN PATENT DOCUMENTS

EP	0 216 479	A1	4/1987	
EP	0 425 066	A1	5/1991	
EP	0 487 404	A1	5/1992	
EP	0 518 772	A1	12/1992	
EP	0 518 773	A1	12/1992	
EP	0 524 109	B1	6/1995	
EP	0 667 145	A1	8/1995	
EP	0 750 899	A2	1/1997	
EP	0 771 795	A1	5/1997	
EP	0 852 949	A2	7/1998	
EP	1 069 142		1/2001	
EP	0 895 779	B1	8/2003	
EP	1 430 883	A1	6/2004	
EP	1 466 590	A1	10/2004	
EP	1 468 674	A1	10/2004	
EP	1 473 024	A1	11/2004	
EP	1 589 010	A1	10/2005	
FR	2 609 397	A1	7/1988	
FR	2 722 380	A1	1/1996	
FR	2 756 735	A1	6/1998	
FR	2 761 959	A1	10/1998	
FR	2 768 623	A1	3/1999	
FR	2 770 776	A1	5/1999	
FR	2 773 324	A1	7/1999	
FR	2 791 042	A1	9/2000	
FR	2 792 618	A1	10/2000	
FR	2 811 565	A1	1/2002	
FR	2 811 993	A1	1/2002	
FR	2 818 547	A1	6/2002	
FR	2 818 646	A1	6/2002	
FR	2 861 729	A1	5/2005	
FR	2 867 684	A1	9/2005	
FR	2 869 317	A1	10/2005	
FR	2 876 283	A1	4/2006	
FR	2 877 220	A1	5/2006	
GB	2 156 799		10/1985	
JP	A-02-295912		12/1990	
WO	WO 93/04665	A1	3/1993	
WO	WO 96/19182	A1	6/1996	
WO	WO 96/19184	A1	6/1996	
WO	WO 98/44012	A1	10/1998	
WO	WO 99/10318	A1	3/1999	
WO	WO 99/22707	A1	5/1999	
WO	WO 99/24009	A1	5/1999	
WO	WO 99/32077	A1	7/1999	
WO	WO 00/68282	A1	11/2000	
WO	WO 01/03538	A1	1/2001	
WO	WO 01/79644	A1	10/2001	
WO	WO 00/31154	A1	6/2002	
WO	WO 02/43677	A2	6/2002	
WO	WO 02/43686	A2	6/2002	
WO	WO 02/43687	A2	6/2002	
WO	WO 02/43688	A2	6/2002	
WO	WO 02/43689	A2	6/2002	
WO	WO 02/44224	A2	6/2002	
WO	WO 02/44225	A2	6/2002	
WO	WO 02/44227	A2	6/2002	
WO	WO 02/44229	A1	6/2002	
WO	WO 02/44230	A2	6/2002	
WO	WO 02/44231	A1	6/2002	
WO	WO 02/44267	A2	6/2002	
WO	WO 02/44268	A1	6/2002	
WO	WO 02/44269	A1	6/2002	
WO	WO 02/44270	A2	6/2002	
WO	WO 02/44271	A2	6/2002	
WO	WO 02/051803	A2	7/2002	
WO	WO02/051828	*	7/2002	..... C07D 309/10
WO	WO 02/051828	A2	7/2002	
WO	WO 03/018423	A1	3/2003	
WO	WO 2004/028483	A2	4/2004	
WO	WO 2004/073759	A1	9/2004	
WO	WO 2006/090307	*	8/2006	..... A61K 8/60
WO	WO 2006/090307	A1	8/2006	

WO	WO 2006/128738	A1	12/2006
WO	WO 2008/148966	A2	12/2008
WO	WO 2009/034559	A2	3/2009

## OTHER PUBLICATIONS

Schafer et al., Failure is an option: learning from unsuccessful proof-of-concept trials, *Drug Discovery Today*, vol. 13, Nos. 21/22, Nov. 2008.\*

Horig et al., From bench to clinic and back: Perspective on the 1st IQPC Translational Research conference, *Journal of Translational Medicine* 2004, 2:44.\*

Jan. 12, 2012 Office Action issued in U.S. Appl. No. 11/822,098.

Office Action issued in U.S. Appl. No. 11/822,160; mailed Oct. 27, 2010.

Office Action issued in U.S. Appl. No. 11/822,107; mailed Jun. 24, 2010.

Office Action issued in U.S. Appl. No. 11/822,098; mailed Jul. 13, 2010.

Egelrud et al., "Proteolytic Degradation of Desmosomes in Plantar Stratum Corneum Leads to Cell Dissociation in vitro," *Acta Derm Venereol.*, vol. 68, pp. 93-97, 1988.

Egelrud et al., "The Dependence of Detergent-Induced Cell Dissociation in Non-Palmo-Plantar Stratum Corneum on Endogenous Proteolysis," *J. Invest Dermatol.*, vol. 95, No. 4, pp. 456-459, Oct. 1990.

Egelrud et al., "A chymotrypsin-like proteinase that may be involved in desquamation in plantar stratum corneum," *Archives of Dermatological Research*, vol. 238, pp. 108-112, 1991.

Walsh et al., "Sugars protect desmosome and comeosome glycoproteins from proteolysis," *Archives of Dermatological Research*, vol. 283, pp. 174-179, 1991.

Brysk et al., "Glycoproteins modulate adhesion in terminally differentiated keratinocytes," *Cell and Tissue Research*, vol. 253, pp. 657-663, 1988.

Brysk et al., "Predesquamin Inhibits Desquamation," *Experimental Cell Research*, vol. 209, pp. 301-306, 1993.

Brysk et al., "Cohesion and desquamation of epidermal stratum corneum," *Prog. Histochem Cytochem.*, vol. 25, pp. 1-53, 1992.

Brysk et al., "Sensitivity of Desquamin to Proteolytic Degradation," *Pathobiology*, vol. 59, pp. 109-112, 1991.

Vicanova et al., "Impaired desquamation in the in vitro reconstructed human epidermis," *Cell & Tissue Research*, vol. 286, pp. 115-122, 1996.

Simon et al., "Persistence of Both Peripheral and Non-Peripheral Comedosomes in the Upper Stratum Corneum of Winter Xerosis Skin Versus only Peripheral in Normal Skin," *Journal of Investigative Dermatology*, vol. 116, No. 1, Jan. 2001.

Imokawa, Genji et al., "Decreased Level of Ceramides in Stratum Corneum of Atopic Dermatitis: An Etiologic Factor in Atopic Dry Skin?" *The Journal of Investigative Dermatology*, 1991, pp. 523-526, vol. 96.

Di Nardo, A. et al., "Ceramide and Cholesterol Composition of the Skin of Patients with Atopic Dermatitis", *Acta Derm Venereol* (Stockh), 1998, pp. 27-30, vol. 78.

Wilmer J. et al., "Cytokine Induction in Human Epidermal Keratinocytes Exposed to Contact Irritants and Its Relation to Chemical-Induced Inflammation in Mouse Skin," *Journal of Investigative Dermatology*, 1994, pp. 915-922, vol. 102.

Morisette, S.L. et al., "High-Throughput Crystallization: Polymorphs, Salts, Co-Crystals and Solvates of Pharmaceutical Solids," *Advanced Drug Delivery Reviews*, 2004, pp. 275-300, vol. 56.

Vippagunta, S.R. et al., "Crystalline Solids," *Advanced Drug Delivery Reviews*, 2001, pp. 3-26, vol. 48.

Allgaier, J., et al., "Synthesis and Characterization of Poly[1,4-isoprene-b-(ethyleneoxide)] and Poly[ethylene-co-propylene-b-(ethylene oxide)] Block Copolymers," *Macromolecules*, 1997, pp. 1582-1586, vol. 30, No. 6.

Morishima, Y. "Self-Assembling Amphiphilic Polyelectrolytes and Their Nanostructures," *Chinese Journal of Polymer Science*, 2000, pp. 323-336, vol. 18, No. 40.

(56)

**References Cited****OTHER PUBLICATIONS**

- Noda, T., et al. "Micelle Formation of Random Copolymers of Sodium 2-(Acrylamido)-2-methylpropanesulfonate and a Nonionic Surfactant Macromonomer in Water as Studied by Fluorescence and Dynamic Light Scattering," *Macromolecules*, 2000, pp. 3694-3704, vol. 33, No. 10.
- Noda, T., et al. "Solution Properties of Micelle Networks Formed by Nonionic Surfactant Moieties Covalently Bound to a Polyelectrolyte: Salt Effects on Rheological Behavior," *Langmuir*, 2000, pp. 5324-5332, vol. 16, No. 12.
- Noda, T., et al. "Stimuli-Responsive Amphiphilic Copolymers of Sodium 2-(Acrylamido)-2-Methylpropanesulfonate and Associative Macromonomers," *Polymer Preprints*, 1999, pp. 220-221, vol. 40, No. 2.
- WordNet Search 3.0, "Prevent," Nov. 14, 2007.
- YourDictionary.com, "Calmativ," Jan. 28, 2010.
- Merriam-Webster Online Dictionary, "Derivative," Jul. 15, 2009.
- MayoClinic, "Hair Loss," Feb. 12, 2010.
- The Merck Manual of Diagnostics and Therapy, Seventeenth Edition, 1999, pp. 788-791.
- U.S. Office Action issued Dec. 29, 2009 in related U.S. Appl. No. 11/822,115.
- U.S. Office Action issued Dec. 11, 2008 in related U.S. Appl. No. 11/822,114.
- U.S. Office Action issued Sep. 30, 2009 in related U.S. Appl. No. 11/822,114.
- U.S. Office Action issued Feb. 4, 2010 in related U.S. Appl. No. 11/822,160.
- U.S. Office Action issued Jan. 7, 2010 in related U.S. Appl. No. 11/822,098.
- U.S. Office Action issued May 13, 2009 in related U.S. Appl. No. 11/783,410.
- U.S. Office Action issued Feb. 3, 2010 in related U.S. Appl. No. 11/783,410.
- U.S. Office Action issued Jun. 24, 2009 in related U.S. Appl. No. 11/783,411.
- U.S. Office Action issued Feb. 3, 2010 in related U.S. Appl. No. 11/783,411.
- International Search Report issued Dec. 10, 2007 in Application No. PCT/FR2007/051587.
- French Search Report issued in French Application No. 0606021, Feb. 15, 2007.
- French Search Report issued in French Application No. 0606025, Feb. 22, 2007.
- French Search Report issued in French Application No. 0606015, May 6, 2005.
- French Search Report issued in French Application No. 0606023, Apr. 4, 2007.
- French Search Report issued in French Application No. 0651269, Dec. 15, 2006.
- May 19, 2011 Restriction and Election of Species Requirement issued in U.S. Appl. No. 12/306,566.
- Sep. 1, 2011 Office Action issued in U.S. Appl. No. 11/822,160.
- Held, E. et al., "Effect of different moisturizers on SLS-irritated human skin", *Contact Dermatitis*, 2001, vol. 44, pp. 299-234.
- MayoClinic.com, "Dry Skin", <http://www.mayoclinic.com/health/dry-skin/DS00560>; last viewed Aug. 25, 2011, seven pages.
- Third Parties Observations issued in European Patent Application No. 07301199.1 dated Nov. 11, 2011.
- Brhat Nighantu Ratnakara (Saligramanighantubhusanam)—Compiled by Gangāvisnu Śrīkṛṣṇa Dāsa, Translated by Sri Dattarama Śrīkṛṣṇalāla Mathura; vol.-4 (Part VII), edn. 1997, Khemaraja Śrīkṛṣṇadas Prakasana, Mumbai-4 [This book contains back references from 1000 B.C. to 20<sup>th</sup> century] p. 370 Formulation ID: RS/4798 Formulation Name: Śatapatrīgūṇāh.
- Sodhala; Sodhalanighantauh-(Nāmasamgraha Va Gunasamgraha) Edited by P.V. Sharma, Oriental Institute, Baroda, Edn 1<sup>st</sup> 1978 p. 136 Formulation ID: RG9/396B Formulation Name: Satapatrika Lepa.
- Rasatantrasārah Evam Siddhaprayogasamgrahah; part II; Krishan Gopal Ayurveda Bhawan; Edn 8<sup>th</sup>; 1990 [This book contains back references from 1000 B.C. to 20<sup>th</sup> century] p. 538 Formulation ID: RS21 / 688 Formulation Name: Akasira Dimaga Taila.
- Rasatantrasārah Evam Siddhaprayogasamgrahah; part II; Krishan Gopal Ayurveda Bhawan; Edn 8<sup>th</sup>; 1990 [This book contains back references from 1000 B.C. to 20<sup>th</sup> century] p. 485-486 Formulation ID: RS21/600 Formulation Name: Pandeya Udvartana.
- Jul. 18, 2012 Office Action issued in U.S. Appl. No. 12/306,566.
- Campoccia et al., "Semisynthetic Resorbable Materials from Hyaluronan Esterification", *Biomaterials* 19; 1998; 2101-2127.
- Stern et al., "Hyaluronan fragments: An information-rich system", *European Journal of Cell Biology*; vol. 85; 2006; pp. 699-715.
- Braga et al., "Making crystals from crystals: a green route to crystal engineering and polymorphism," *Chem. Commun.*, 2005; 3635-3645.
- General Chemistry Online Dictionary, "lipid"; also available at <http://antoine.frostburg.edu/chem/senese/101/glossary/l.shtml>; last accessed Apr. 25, 2012.
- SciFinder, "Jjoba Oil"; last accessed Apr. 25, 2012.
- May 3, 2012 Office Action issued in U.S. Appl. No. 11/822,160.
- U.S. Appl. No. 12/192,698 in the name of Bissey et al., filed Aug. 15, 2008.
- U.S. Appl. No. 12/649,366 in the name of Laboureau et al., filed Dec. 30, 2009.
- U.S. Appl. No. 12/704,978 in the name of Breton et al., filed Feb. 12, 2010.
- U.S. Appl. No. 11/822,098 in the name of Pineau et al., Jul. 2, 2007.
- U.S. Appl. No. 11/822,160 in the name of Willemine et al., filed Jul. 2, 2007.
- U.S. Appl. No. 12/306,566 in the name of Pineau et al., filed Feb. 26, 2009.
- Hilda Butler, "Poucher's Perfumes, Cosmetics and Soaps," 2000, Kluwer Academic Publishers, 10<sup>th</sup> Edition, pp. 403-405.
- The Merriam-Webster Online Dictionary, obtained online at: <http://www.merriam-webster.com/dictionary/prevent>, downloaded on Jan. 24, 2012, 2 pages.
- The Merriam-Webster Online Dictionary, obtained online at: <http://www.merriam-webster.com/dictionary/cure>, downloaded on Jan. 24, 2012, 2 pages.
- The Merriam-Webster Online Dictionary, obtained online at: <http://www.merriam-webster.com/dictionary/derivative>, downloaded on Jul. 5, 2008, 1 page.
- Wermuth, *Drug Discovery Today*, 2006, vol. 11, Nos. 7/8, pp. 348-354.
- Jan. 30, 2012 Office Action issued in U.S. Appl. No. 12/306,566.
- Jul. 31, 2013 Office Action issued in U.S. Appl. No. 12/306,566.
- Apr. 15, 2014 Office Action issued in U.S. Appl. No. 12/306,566.

\* cited by examiner

## USE OF C-GLYCOSIDE DERIVATIVES AS PRO-DESQUAMATING ACTIVE AGENTS

The invention relates to the cosmetic use of at least one C-glycoside derivative in a composition, especially a cosmetic composition, comprising a physiologically acceptable medium, as an agent for promoting desquamation of the skin and/or the scalp and/or for stimulating epidermal renewal.

The C-glycoside derivative according to the present invention may be used for cosmetic and/or therapeutic purposes, provided that it is used as an active agent for stimulating desquamation, also known as a pro-desquamating active agent.

Desquamation is a natural phenomenon associated with the fact that the epidermis, which constitutes the upper layer of the skin, is in constant regeneration.

The epidermis consists of several layers of cells, the deepest of which is the basal layer consisting of undifferentiated cells. Over time, these cells differentiate and migrate towards the surface of the epidermis, forming the various layers thereof, until they form at the surface of the epidermis the corneocytes, which are dead cells that become removed by desquamation. This surface loss is compensated for by the migration of cells from the basal layer to the surface of the epidermis. This constitutes a perpetual renewal of the skin.

The corneocytes are mainly composed of a fibrous matrix containing cytokeratins, surrounded by a very strong structure 15 nm thick, known as the horny or cornified envelope. The stacking of these corneocytes constitutes the horny layer, which is responsible for the barrier function of the epidermis. During the normal process of desquamation, the uppermost corneocytes become detached from the surface of the epidermis.

Intercellular structures derived from desmosomes, known as corneosomes or corneodesmosomes, have been described in the horny layer. Recent studies have shown their major importance in intercorneocytic cohesion and also in the desquamation process.

The gradual appearance of fragments of desmosomal proteins during the differentiation and also the ultrastructural changes of the desmosome put research workers on the track of enzymes responsible for these changes. The first, Egelrud and Lundström (Egelrud, Hofer et al. 1988 *Acta Derm. Venereol.* 68:93-97; Egelrud and Lundström 1990, *J. Invest. Dermatol.* 95: 456-459; Egelrud and Lundström, 1991, *Arch. Dermatol. Res.* 283: 108-112), have demonstrated in the stratum corneum the existence of protease activities of "trypsin-like" and above all "chymotrypsin-like" type associated with desquamation. Several cysteine proteases and aspartic acid proteases are now assumed to be involved in this process: "stratum corneum thiol protease" (SCTP), cathepsin E and cathepsin D.

Walsh and Chapman (Walsh and Chapman, 1991; *Arch. Dermatol. Res.* 283: 174-179) have shown that desquamation is the result of the action of at least two classes of enzymes on the intercorneocytic bonds. They have observed that the proteases cannot act alone and that a prior action of glycosidases that demask the sites of proteolysis is necessary. The experiments they performed confirmed that glycoproteins play a major role in cohesion. One particular glycoprotein has been described in relation with desquamation, and named desquamine. It is a 40 kDa glycoprotein located in the upper part of the stratum corneum, and which was isolated by Brysk et al. (Brysk et al. 1988; *Cell Tissue Res.* 253: 657-663). Its precursor, predesquamine (600 kDa), is believed to be located in the deep layers the stratum corneum

and in the stratum granulosum (SG). M. Brysk showed, by using the desquamation model of T. Egelrud, that this precursor inhibits desquamation in a dose-dependent manner at very low concentrations, of nanomolar order (Brysk et al., 1993; *Exp. Cell Res.* 209: 301-306). It is thus thought to play an important role in blocking early desquamation. Its degradation in the SG/stratum corneum interzone and in the upper part of the stratum corneum generates desquamine, which in turn is believed to modify desquamation (Brysk and Rajaraman, 1992; *Prog. Histochem. Cytochem.* 25: 1-53). Desquamine is capable in vitro of causing haemagglutinations, which clearly proves its nature as an endogenous lectin. It is not competitively inhibited until sugar concentrations of millimolar order, whereas the other lectins are competitively inhibited for concentrations below 50 micromolar (Brysk et al., 1988). This lectin bonds the amino-sugars of adjacent cells by bridging. The use of an anti-desquamine monoclonal antibody for inhibiting the in vitro reaggregation of the corneocytes demonstrates the possible role of desquamine in cohesion.

Reaggregation is also inhibited by the addition of amino-sugars that bind to the endogenous lectins and by the addition of exogenous lectins specific for the amino-sugars, which bind the ligand (Brysk et al. 1988). Some of these sugars have been claimed as pro-desquamating active agents. Finally, desquamine is resistant in vitro to the majority of the proteases described in the stratum corneum. This situation is reinforced in vivo, since its presence, in the lipid mortar of the spaces, protects its sites of enzymatic cleavage (Brysk et al., 1991; *Pathobiology* 59: 109-112).

The present invention is more particularly focused on treating the signs associated with desquamation disorders.

Deregulations of desquamation are increasingly well described at the molecular level and are associated with veritable pathologies of the type such as ichthyosis, psoriasis, atopic dermatitis and xerosis, for example, or with abnormal skin aspects.

Thus, in a certain number of situations, it may be desired to stimulate this desquamation mechanism in order to promote epidermal renewal, to attenuate surface irregularities and to make the skin smooth, or to promote the cleansing action and the removal of dead cells at the surface of the body.

In certain physiological conditions, thickening of the horny layer is also observed, which it is desired to limit, for example in the case of calluses or after exposure to sunlight.

In certain skin disorders, the desquamation becomes visible and large squamae comprising numerous corneocytes are removed.

In the field of acne, the accumulation of a keratinous plug (which may be removed by the activity of proteases) blocking the pores is one of the reasons for the appearance of comedones.

The appearance of dandruff is another example of a desquamation defect in which the squamae are abnormally visible.

Genetic defects at the level of proteases and of protease inhibitors are also associated with the appearance of hyperkeratotic or ichthyotic phenotypes.

The impaired desquamation that is generally present in reconstructed epidermides (Vicanova, Mommaas et al. 1996) also represents a proteolytic defect.

Certain pathological skin types may also benefit from pro-desquamating treatment. Among these pathologies, mention is made of Netherton's syndrome, Papillon-Lefèvre syndrome and more generally ichthyoses of genetic origin and also psoriasis or atopic dermatitis.

In the field of normal but impaired skin in which there is deregulation of desquamation, mention may be made of various xeroses (Simon et al., 2001; *J. Invest. Dermatol.* 116: 23-30), whether they are senile or winter-related, associated with the onset of the menopause or with the exaggerated use of certain detergents.

Thus, the present patent application is also directed towards desquamation disorders that can be remedied by means of solutions belonging to the field of cosmetics. In particular, in this respect, means may be sought for homogenizing the skin relief, for removing surface roughness to produce a smoothing effect, for improving the radiance of the complexion, for improving the staying power of makeup, for improving the efficacy of peeling treatments or for preparing the skin before the application of a self-tanning agents such as dihydroxyacetone (DHA).

Certain cosmetic agents are known to promote desquamation, i.e. the removal of "dead" cells at the surface of the horny layer of the epidermis. In this respect, mention may be made especially of  $\alpha$ -hydroxy acids (AHAs), for instance lactic acid or glycolic acid, or  $\beta$ -hydroxy acids (BHAs), for instance salicylic acid. However, these desquamating agents may be criticized for being liable to cause undesirable local irritation.

There is thus a need to find pro-desquamating agents that can be implemented for their use against the abovementioned skin disorders, whether they are of dermatological nature or correspond more to concerns of a cosmetic nature also mentioned above, and free of the drawbacks described previously.

The inventors have discovered, surprisingly, that certain C-glycoside derivatives are advantageous in precisely this respect.

Sugars and sugar derivatives are products that have already been exploited for various purposes for the formulation of cosmetic compositions intended either for skincare or for caring for and/or washing keratin fibres.

Among these sugars, C-glycoside derivatives prove to be most particularly advantageous. Thus, certain C-glycoside derivatives have demonstrated advantageous biological properties, in particular for combating ageing of the epidermis and/or dryness of the skin. Such compounds are especially described in document WO 02/051 828.

The invention results more particularly from the observation by the inventors that C-glycoside derivatives show pro-desquamating properties.

Thus, according to one of its aspects, the invention relates to the cosmetic use of at least one C-glycoside derivative in a composition, especially a cosmetic composition, comprising a physiologically acceptable medium, as a cosmetic agent for promoting desquamation of the skin and/or the scalp and/or for stimulating epidermal renewal.

Such a composition is more particularly useful for improving the appearance and/or texture of the skin and/or the scalp.

According to one of its advantages, a composition according to the invention shows desquamating properties without inducing local irritation.

In particular, the present invention relates to the cosmetic use of at least one C-glycoside derivative in a composition, especially a cosmetic composition, comprising a physiologically acceptable medium, the said composition being intended for combating keratosis and imperfections of acne-prone greasy skin, for combating the formation of dandruff, for homogenizing the skin relief, for removing surface roughness to afford a smoothing effect, for reducing surface irregularities and the skin's microrelief, for improving the

radiance of the complexion, for improving the staying power of makeup, for improving the efficacy of peeling treatments, or for preparing the skin before the application of a self-tanning agent such as dihydroxyacetone (DHA) and/or for improving the result of a skin treatment with stratum corneum colorants such as dihydroxyacetone (DHA).

More generally, it is understood that the cosmetic use according to the present invention makes it possible to improve the appearance and/or texture of the skin and/or the scalp.

As regards greasy skin, this is often associated with a desquamation defect, and with a thick skin grain. Furthermore, the excess sebum may serve as a support for the anarchic growth of saprophytic bacterial flora (in particular *Propionibacterium acnes* and *Pityrosporum ovale*), and cause the appearance of comedones and/or acne scars. These acne scars are another cutaneous sign of greasy skin that may advantageously be combated by means of the use of a C-glycoside according to the present invention.

The invention also relates to cosmetic processes for treating the skin and/or its appendages, for the purpose of stimulating desquamation and/or exfoliation and/or cell renewal, and to compositions for implementing them.

According to another of its aspects, a subject of the invention is the use of at least one C-glycoside derivative for the preparation of a composition for preventing and/or treating signs associated with desquamation disorders.

In particular, the invention also relates to the use of at least one C-glycoside derivative for the preparation of a composition for preventing and/or treating skin and/or scalp disorders linked to deregulation of desquamation, especially when it is associated with the production of a thick horny layer and/or with abnormal desquamation.

Many skin pathologies are characterized by the production of a thickened horny layer and by abnormal desquamation, i.e. hyperkeratosis. This may occur on any anatomical region of skin and in very varied clinical contexts. Its physiopathological substratum and its cause are varied.

Advantageously, the C-glycoside derivatives in accordance with the invention make it possible to promote desquamation of the skin and/or to stimulate epidermal renewal and thus, more particularly, to treat skin and/or scalp pathologies that are characterized by the production of a thickened horny layer and/or by abnormal desquamation.

Consequently, according to another of its aspects, the present invention also relates to the use of a C-glycoside derivative for the preparation of a composition for treating skin and/or scalp pathologies characterized by the production of a thickened horny layer and/or by abnormal desquamation.

As non-limiting illustrations of these skin and/or scalp disorders associated with deregulation of desquamation, mention may be made, in the context of the present invention, of:

- xerosis,
- acne,
- hyperkeratosis,
- psoriasis,
- atopy,
- ichthyosis, and
- certain benign or malignant tumour lesions.

According to another of its aspects, the present invention relates to a cosmetic treatment process for promoting desquamation and/or for stimulating epidermal renewal, characterized in that it comprises the application to the skin

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and/or the scalp of a composition comprising, in a physiologically acceptable medium, at least one C-glycoside derivative.

Advantageously, the cosmetic treatment process is suitable for skin displaying keratosis, acne-prone greasy skin, skin with rough areas or skin with a thick skin grain.

Another subject of the invention is a cosmetic treatment process for improving the radiance of the complexion and/or for reducing surface irregularities of the skin and/or of mucous membranes, characterized in that at least one C-glycoside derivative, or a composition containing it, is applied to the skin or the mucous membranes.

For the implementation of this process, the C-glycoside derivative or the composition containing it may be applied to any area of skin or of its appendages, especially of the face, the neckline or the hands, or to the lips, in order to attenuate visible and/or tactile skin irregularities, for example to attenuate scars, to make the surface smooth and/or to remove dead skin especially from the lips.

According to another embodiment, the invention relates to a cosmetic process for promoting desquamation of the skin and/or mucous membranes, comprising at least one step (i) of preparing the skin for a peeling treatment, which consists in applying to the areas to be treated at least one C-glycoside derivative, at least at a concentration lower than that resulting in desquamation, and (ii) a subsequent step comprising the application of at least one desquamating agent at a concentration suitable for causing desquamation. A step of removing the desquamating agent(s) by rinsing will then be performed.

Advantageously, step (i) may be repeated with increasing concentrations of C-glycoside. These concentrations will be adapted by a person skilled in the art as a function of the desired effect and of the intended number of applications, but will generally be less than 10%. It may be possible, for example, to use a first concentration of about 2%, and then one or more successive applications with a concentration of about 4%, and then 6% or 8% by weight.

According to another of its aspects, the invention relates to a cosmetic process for treating keratin materials, which consists in applying at least two components:

a first component comprising at least one C-glycoside derivative or a composition containing it, especially as defined below,

a second component comprising at least one agent chosen from proteases, lipases and glycosidases, these two components being applied simultaneously, in combination or sequentially to the skin, mucous membranes or the scalp.

According to one particular embodiment, these two components may be formulated in different compositions.

Advantageously, the second component will comprise at least one protease, involved in desquamation.

Agents chosen from moisturizers, agents that reduce or inhibit the activity of harmful proteases, agents that stimulate epidermal differentiation and anti-seborrheic agents may advantageously be present in the first and/or second component.

Another subject of the invention is the use of at least one C-glycoside derivative as defined hereinbelow, for the preparation of reconstructed skin.

The invention thus relates to a process for prolonging the lifetime of reconstructed skin in vitro, and more particularly reconstructed epidermides.

According to one of the embodiments, the reconstructed epidermis may be treated daily with low concentrations of a C-glycoside derivative such as C-β-D-xylopyranoside-2-

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hydroxypropane and derivatives thereof, in order to promote regular desquamation similar to that observed in the case of healthy skin in vivo.

According to another embodiment variant, the C-glycoside derivative, especially C-β-D-xylopyranoside-2-hydroxypropane may be spot-applied to a reconstructed epidermis, at a high dose similar to that of a peeling treatment, i.e. about 20% to 40% by weight relative to the weight of the composition, and then removed by rinsing. This process makes it possible to remove the constituted horny layer or a part thereof whose accumulation may be harmful to the survival of the keratinocytes.

#### C-Glycoside Derivatives

A C-glycoside derivative that is suitable for use in the invention may be a compound of general formula (I) below:



in which:

R represents:

a saturated C<sub>1</sub>-C<sub>20</sub> and in particular C<sub>1</sub>-C<sub>10</sub> or unsaturated C<sub>2</sub>-C<sub>20</sub> and in particular C<sub>2</sub>-C<sub>10</sub> linear alkyl radical, or a saturated or unsaturated, branched or cyclic C<sub>3</sub>-C<sub>20</sub> and in particular C<sub>3</sub>-C<sub>10</sub> alkyl radical;

a saturated C<sub>1</sub>-C<sub>20</sub> and in particular C<sub>1</sub>-C<sub>10</sub> or unsaturated C<sub>2</sub>-C<sub>20</sub> linear, and in particular C<sub>2</sub>-C<sub>10</sub>, or saturated or unsaturated, branched or cyclic C<sub>3</sub>-C<sub>20</sub> and in particular C<sub>3</sub>-C<sub>10</sub> linear hydrofluoroalkyl or perfluoroalkyl radical;

the hydrocarbon-based chain constituting the said radicals possibly being, where appropriate, interrupted with 1, 2, 3 or more heteroatoms chosen from:

an oxygen,  
a sulfur,  
a nitrogen, and  
a silicon,

and possibly being optionally substituted with at least one radical chosen from:

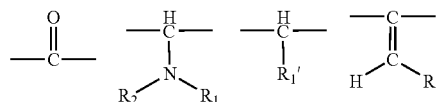
—OR<sub>4</sub>,  
—SR<sub>4</sub>,  
—NR<sub>4</sub>R<sub>5</sub>,  
—COOR<sub>4</sub>,  
—CONR<sub>4</sub>R<sub>5</sub>,  
—CN,

a halogen atom,

a C<sub>1</sub>-C<sub>6</sub> hydrofluoroalkyl or perfluoroalkyl radical, and/or a C<sub>3</sub>-C<sub>8</sub> cycloalkyl radical,

with R<sub>4</sub> and R<sub>5</sub> possibly representing, independently of each other, a hydrogen atom or a saturated C<sub>1</sub>-C<sub>30</sub> and in particular C<sub>1</sub>-C<sub>12</sub> or unsaturated C<sub>2</sub>-C<sub>30</sub> linear, and in particular C<sub>2</sub>-C<sub>12</sub>, or a saturated or unsaturated, branched or cyclic C<sub>3</sub>-C<sub>30</sub> and in particular C<sub>3</sub>-C<sub>12</sub> alkyl, perfluoroalkyl or hydrofluoroalkyl radical; or a C<sub>6</sub>-C<sub>10</sub> aryl radical,

X represents a radical chosen from the groups:



with R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> representing, independently of each other, a hydrogen atom or a radical R, with R as defined

above, and R<sub>1</sub> represents a hydrogen atom, an —OH group or a radical R as defined above, R<sub>1</sub> possibly also denoting a C<sub>6</sub>-C<sub>10</sub> aryl radical;

S represents a monosaccharide or a polysaccharide comprising up to 20 sugar units and in particular up to 6 sugar units, in pyranose and/or furanose form and of L and/or D series, the said mono- or polysaccharide possibly being substituted with a mandatorily free hydroxyl group, and optionally one or more optionally protected amine function(s), and

the bond S—CH<sub>2</sub>—X represents a bond of C-anomeric nature, which may be α or β, and also the cosmetically acceptable salts thereof, the solvates thereof such as hydrates, and the isomers thereof.

In the context of the present invention, the term “halogen” means chlorine, fluorine or bromine.

The term “aryl” denotes an aromatic ring such as phenyl, optionally substituted with one or more C<sub>1</sub>-C<sub>4</sub> alkyl radicals.

The term “C<sub>3</sub>-C<sub>8</sub> cycloalkyl” denotes an aliphatic ring containing from 3 to 8 carbon atoms, for example including cyclopropyl, cyclopentyl and cyclohexyl.

Among the alkyl groups that are suitable for use in the invention, mention may be made especially of methyl, ethyl, isopropyl, n-propyl, n-butyl, t-butyl, isobutyl, sec-butyl, pentyl, n-hexyl, cyclopropyl, cyclopentyl, cyclohexyl and allyl groups.

According to one embodiment of the invention, it is possible to use a C-glycoside derivative corresponding to formula (I) for which S may represent a monosaccharide or a polysaccharide containing up to 6 sugar units, in pyranose and/or furanose form and of L and/or D series, the said monosaccharide or polysaccharide containing at least one hydroxyl function that is mandatorily free and/or optionally one or more amine functions that are mandatorily protected, X and R otherwise retaining all the definitions given above.

Advantageously, a monosaccharide of the invention may be chosen from D-glucose, D-galactose, D-mannose, D-xylose, D-lyxose, L-fucose, L-arabinose, L-rhamnose, D-glucuronic acid, D-galacturonic acid, D-iduronic acid, N-acetyl-D-glucosamine and N-acetyl-D-galactosamine, and advantageously denotes D-glucose, D-xylose, N-acetyl-D-glucosamine or L-fucose, and in particular D-xylose.

More particularly, a polysaccharide of the invention containing up to 6 sugar units may be chosen from D-maltose, D-lactose, D-cellobiose, D-maltotriose, a disaccharide combining a uronic acid chosen from D-iduronic acid and D-glucuronic acid with a hexosamine chosen from D-galactosamine, D-glucosamine, N-acetyl-D-galactosamine and N-acetyl-D-glucosamine, an oligosaccharide containing at least one xylose advantageously chosen from xylobiose, methyl-β-xylobioside, xylotriose, xylotetraose, xylopentaose and xylohexaose and especially xylobiose, which is composed of two xylose molecules linked via a 1-4 bond.

More particularly, S may represent a monosaccharide chosen from D-glucose, D-xylose, L-fucose, D-galactose and D-maltose, especially D-xylose.

According to another embodiment of the invention, it is possible to use C-glycoside derivatives corresponding to formula (I) for which X represents a group chosen from —CO—, —CH(OH)—, —CH(NR<sub>1</sub>R<sub>2</sub>)— and —CH(R)—, in particular —CO—, —CH(OH)—, —CH(NH<sub>2</sub>)—, —CH(NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH)—, —CH(NHPh)— and —CH(CH<sub>3</sub>)—, and more particularly a —CO—, —CH(OH)— or —CH(NH<sub>2</sub>)— group, and preferentially a —CH(OH)— group, S and R otherwise conserving all of the definitions given above.

According to another embodiment of the invention, it is possible to use a C-glycoside derivative corresponding to formula (I) for which R represents a saturated C<sub>1</sub>-C<sub>20</sub> and in particular C<sub>1</sub>-C<sub>10</sub> or unsaturated C<sub>2</sub>-C<sub>10</sub> and in particular C<sub>2</sub>-C<sub>10</sub> linear alkyl radical, or a saturated or unsaturated, branched or cyclic C<sub>3</sub>-C<sub>20</sub> and in particular C<sub>3</sub>-C<sub>10</sub> alkyl radical; and optionally substituted as described above, S and X otherwise conserving all the definitions given above. Preferably, R denotes a linear C<sub>1</sub>-C<sub>4</sub> and especially C<sub>1</sub>-C<sub>3</sub> radical, optionally substituted with —OH, —COOH or —COOR<sup>2</sup>, R<sup>2</sup> being a saturated C<sub>1</sub>-C<sub>4</sub> alkyl radical, especially ethyl.

Preferentially, R denotes an unsubstituted linear C<sub>1</sub>-C<sub>4</sub> and especially C<sub>1</sub>-C<sub>2</sub> alkyl radical, in particular ethyl.

Among the C-glycoside derivatives of formula (I) that are preferably used are those for which:

R represents a saturated C<sub>1</sub>-C<sub>20</sub> and in particular C<sub>1</sub>-C<sub>10</sub> or unsaturated C<sub>1</sub>-C<sub>20</sub> and in particular C<sub>2</sub>-C<sub>10</sub> linear alkyl radical, or a saturated or unsaturated, branched or Cyclic C<sub>3</sub>-C<sub>20</sub> and in particular C<sub>3</sub>-C<sub>10</sub> alkyl radical, optionally substituted as described above;

S represents a monosaccharide as described above;

X represents —CO—, —CH(OH)—, —CH(NR<sub>1</sub>R<sub>2</sub>)— or —CH(R)—, as defined above.

Preferably, a C-glycoside derivative of formula (I) is used, for which:

R denotes a linear C<sub>1</sub>-C<sub>4</sub> and especially C<sub>1</sub>-C<sub>3</sub> radical, optionally substituted with —OH, —COOH or —COOR<sup>2</sup>, R<sup>2</sup> being a saturated C<sub>1</sub>-C<sub>4</sub> alkyl radical, especially ethyl;

S represents a monosaccharide as described above;

X represents a group chosen from —CO—, —CH(OH)—, —CH(NH<sub>2</sub>)—, —CH(NHCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH)—, —CH(NHPh)— and —CH(CH<sub>3</sub>)—, and more particularly a —CO—, —CH(OH)— or —CH(NH<sub>2</sub>)— group, and in particular a —CH(OH)— group.

Preferentially, a C-glycoside derivative of formula (I) is used, for which:

R denotes an unsubstituted linear C<sub>1</sub>-C<sub>4</sub> and especially C<sub>1</sub>-C<sub>2</sub> alkyl radical, in particular ethyl;

S represents a monosaccharide as described above; especially D-glucose, D-xylose, N-acetyl-D-glucosamine or L-fucose, in particular D-xylose;

X represents a group chosen from —CO—, —CH(OH)— and —CH(NH<sub>2</sub>)— and preferentially a CH(OH)— group.

The salts that are acceptable for the non-therapeutic use of the compounds described in the present invention comprise conventional non-toxic salts of the said compounds such as those formed from organic or inorganic acids. Examples that may be mentioned include the salts of mineral acids, such as sulfuric acid, hydrochloric acid, hydrobromic acid, hydriodic acid, phosphoric acid or boric acid. Mention may also be made of the salts of organic acids, which may comprise one or more carboxylic, sulfonic or phosphonic groups. They may be linear, branched or cyclic aliphatic acids or alternatively aromatic acids. These acids may also comprise one or more heteroatoms chosen from O and N, for example in the form of hydroxyl groups. Mention may be made especially of propionic acid, acetic acid, terephthalic acid, citric acid and tartaric acid.

When the compound of formula (I) comprises an acid group, neutralization of the acid group(s) may be performed with a mineral base, such as LiOH, NaOH, KOH, Ca(OH)<sub>2</sub>, NH<sub>4</sub>OH, Mg(OH)<sub>2</sub> or Zn(OH)<sub>2</sub>; or with an organic base such as a primary, secondary or tertiary alkylamine, for example triethylamine or butylamine. This primary, secondary or tertiary alkylamine may comprise one or more nitrogen and/or oxygen atoms and may thus comprise, for

example, one or more alcohol functions; mention may be made especially of amino-2-methyl-2-propanol, triethanolamine, dimethylamino-2-propanol or 2-amino-2-(hydroxymethyl)-1,3-propanediol. Mention may also be made of lysine or 3-(dimethylamino)propyl amine.

The solvates that are acceptable for the compounds described in the present invention comprise conventional solvates such as those formed during the final step of preparation of the said compounds due to the presence of solvents. Examples that may be mentioned include the solvates due to the presence of water or of linear or branched alcohols, for instance ethanol or isopropanol.

Among the C-glycoside derivatives of formula (I) used according to the invention, the ones that are most particularly considered are:

1. C- $\beta$ -D-xylopyranoside-n-propan-2-one;
2. C- $\alpha$ -D-xylopyranoside-n-propan-2-one;
3. 1-[2-(3-hydroxypropylamino)propyl]-C- $\beta$ -D-xylopyranose;
4. 1-[2-(3-hydroxypropylamino)propyl]-C- $\alpha$ -D-xylopyranose;
5. C- $\beta$ -D-xylopyranoside-2-hydroxypropane;
6. C- $\alpha$ -D-xylopyranoside-2-hydroxypropane;
7. C- $\beta$ -D-xylopyranoside-2-aminopropane;
8. C- $\alpha$ -D-xylopyranoside-2-aminopropane;
9. C- $\beta$ -D-xylopyranoside-2-phenylaminopropane;
10. C- $\alpha$ -D-xylopyranoside-2-phenylaminopropane;
11. ethyl 3-methyl-4-(C- $\beta$ -D-xylopyranoside)butyrate;
12. ethyl 3-methyl-4-(C- $\alpha$ -D-xylopyranoside)butyrate;
13. 6-(C- $\beta$ -D-xylopyranoside)-5-ketohexanoic acid;
14. 6-(C- $\alpha$ -D-xylopyranoside)-5-ketohexanoic acid;
15. 6-(C- $\beta$ -D-xylopyranoside)-5-hydroxyhexanoic acid;
16. 6-(C- $\alpha$ -D-xylopyranoside)-5-hydroxyhexanoic acid;
17. 6-(C- $\beta$ -D-xylopyranoside)-5-aminohexanoic acid;
18. 6-(C- $\alpha$ -D-xylopyranoside)-5-aminohexanoic acid;
19. 6-(C- $\beta$ -D-xylopyranoside)-5-phenylaminohexanoic acid;
20. 6-(C- $\alpha$ -D-xylopyranoside)-5-phenylaminohexanoic acid;
21. 1-(C- $\beta$ -D-xylopyranoside)hexane-2,6-diol;
22. 1-(C- $\alpha$ -D-xylopyranoside)hexane-2,6-diol;
23. 5-(C- $\beta$ -D-xylopyranoside)-4-ketopentanoic acid;
24. 5-(C- $\alpha$ -D-xylopyranoside)-4-ketopentanoic acid;
25. 5-(C- $\beta$ -D-xylopyranoside)-4-hydroxypentanoic acid;
26. 5-(C- $\alpha$ -D-xylopyranoside)-4-hydroxypentanoic acid;
27. 5-(C- $\beta$ -D-xylopyranoside)-4-aminopentanoic acid;
28. 5-(C- $\alpha$ -D-xylopyranoside)-4-aminopentanoic acid;
29. 5-(C- $\beta$ -D-xylopyranoside)-4-phenylaminopentanoic acid;
30. 5-(C- $\alpha$ -D-xylopyranoside)-4-phenylaminopentanoic acid;
31. 1-(C- $\beta$ -D-xylopyranoside)pentane-2,5-diol;
32. 1-(C- $\alpha$ -D-xylopyranoside)pentane-2,5-diol;
33. 1-(C- $\beta$ -D-fucopyranoside)propan-2-one;
34. 1-(C- $\alpha$ -D-fucopyranoside)propan-2-one;
35. 1-(C- $\beta$ -L-fucopyranoside)propan-2-one;
36. 1-(C- $\alpha$ -L-fucopyranoside)propan-2-one;
37. 1-(C- $\beta$ -D-fucopyranoside)-2-hydroxypropane;
38. 1-(C- $\alpha$ -D-fucopyranoside)-2-hydroxypropane;
39. 1-(C- $\beta$ -L-fucopyranoside)-2-hydroxypropane;
40. 1-(C- $\alpha$ -L-fucopyranoside)-2-hydroxypropane;
41. 1-(C- $\beta$ -D-fucopyranoside)-2-aminopropane;
42. 1-(C- $\alpha$ -D-fucopyranoside)-2-aminopropane;
43. 1-(C- $\beta$ -L-fucopyranoside)-2-aminopropane;
44. 1-(C- $\alpha$ -L-fucopyranoside)-2-aminopropane;
45. 1-(C- $\beta$ -D-fucopyranoside)-2-phenylaminopropane;
46. 1-(C- $\alpha$ -D-fucopyranoside)-2-phenylaminopropane;

47. 1-(C- $\beta$ -L-fucopyranoside)-2-phenylaminopropane;
48. 1-(C- $\alpha$ -L-fucopyranoside)-2-phenylaminopropane;
49. ethyl 3-methyl-4-(C- $\beta$ -D-fucopyranoside)butyrate;
50. ethyl 3-methyl-4-(C- $\alpha$ -D-fucopyranoside)butyrate;
51. ethyl 3-methyl-4-(C- $\beta$ -L-fucopyranoside)butyrate;
52. ethyl 3-methyl-4-(C- $\alpha$ -L-fucopyranoside)butyrate;
53. 6-(C- $\beta$ -D-fucopyranoside)-5-ketohexanoic acid;
54. 6-(C- $\alpha$ -D-fucopyranoside)-5-ketohexanoic acid;
55. 6-(C- $\beta$ -L-fucopyranoside)-5-ketohexanoic acid;
56. 6-(C- $\alpha$ -L-fucopyranoside)-5-ketohexanoic acid;
57. 6-(C- $\beta$ -D-fucopyranoside)-5-hydroxyhexanoic acid;
58. 6-(C- $\alpha$ -D-fucopyranoside)-5-hydroxyhexanoic acid;
59. 6-(C- $\beta$ -L-fucopyranoside)-5-hydroxyhexanoic acid;
60. 6-(C- $\alpha$ -L-fucopyranoside)-5-hydroxyhexanoic acid;
61. 6-(C- $\beta$ -D-fucopyranoside)-5-aminohexanoic acid;
62. 6-(C- $\alpha$ -D-fucopyranoside)-5-aminohexanoic acid;
63. 6-(C- $\beta$ -L-fucopyranoside)-5-aminohexanoic acid;
64. 6-(C- $\alpha$ -L-fucopyranoside)-5-aminohexanoic acid;
65. 1-(C- $\beta$ -D-fucopyranoside)hexane-2,6-diol;
66. 1-(C- $\alpha$ -D-fucopyranoside)hexane-2,6-diol;
67. 1-(C- $\beta$ -L-fucopyranoside)hexane-2,6-diol;
68. 1-(C- $\alpha$ -L-fucopyranoside)hexane-2,6-diol;
69. 5-(C- $\beta$ -D-fucopyranoside)-4-ketopentanoic acid;
70. 5-(C- $\alpha$ -D-fucopyranoside)-4-ketopentanoic acid;
71. 5-(C- $\beta$ -L-fucopyranoside)-4-ketopentanoic acid;
72. 5-(C- $\alpha$ -L-fucopyranoside)-4-ketopentanoic acid;
73. 5-(C- $\beta$ -D-fucopyranoside)-4-aminopentanoic acid;
74. 5-(C- $\alpha$ -D-fucopyranoside)-4-aminopentanoic acid;
75. 5-(C- $\beta$ -L-fucopyranoside)-4-aminopentanoic acid;
76. 5-(C- $\alpha$ -L-fucopyranoside)-4-aminopentanoic acid;
77. 5-(C- $\beta$ -D-fucopyranoside)-4-aminopentanoic acid;
78. 5-(C- $\alpha$ -D-fucopyranoside)-4-aminopentanoic acid;
79. 5-(C- $\beta$ -L-fucopyranoside)-4-aminopentanoic acid;
80. 5-(C- $\alpha$ -L-fucopyranoside)-4-aminopentanoic acid;
81. 1-(C- $\beta$ -D-fucopyranoside)pentane-2,5-diol;
82. 1-(C- $\alpha$ -D-fucopyranoside)pentane-2,5-diol;
83. 1-(C- $\beta$ -L-fucopyranoside)pentane-2,5-diol;
84. 1-(C- $\alpha$ -L-fucopyranoside)pentane-2,5-diol;
85. 1-(C- $\beta$ -D-glucopyranosyl)-2-hydroxypropane;
86. 1-(C- $\alpha$ -D-glucopyranosyl)-2-hydroxypropane;
87. 1-(C- $\beta$ -D-glucopyranosyl)-2-aminopropane;
88. 1-(C- $\alpha$ -D-glucopyranosyl)-2-aminopropane;
89. 1-(C- $\beta$ -D-glucopyranosyl)-2-phenylaminopropane;
90. 1-(C- $\alpha$ -D-glucopyranosyl)-2-phenylaminopropane;
91. ethyl 3-methyl-4-(C- $\alpha$ -D-glucopyranosyl)butyrate;
92. ethyl 3-methyl-4-(C- $\alpha$ -D-glucopyranosyl)butyrate;
93. 6-(C- $\beta$ -D-glucopyranosyl)-5-ketohexanoic acid;
94. 6-(C- $\alpha$ -D-glucopyranosyl)-5-ketohexanoic acid;
95. 6-(C- $\beta$ -D-glucopyranosyl)-5-hydroxyhexanoic acid;
96. 6-(C- $\alpha$ -D-glucopyranosyl)-5-hydroxyhexanoic acid;
97. 6-(C- $\beta$ -D-glucopyranosyl)-5-aminohexanoic acid;
98. 6-(C- $\alpha$ -D-glucopyranosyl)-5-aminohexanoic acid;
99. 6-(C- $\beta$ -D-glucopyranosyl)-5-phenylaminohexanoic acid;
100. 6-(C- $\alpha$ -D-glucopyranosyl)-5-phenylaminohexanoic acid;
101. 1-(C- $\beta$ -D-glucopyranosyl)hexane-2,6-diol;
102. 1-(C- $\alpha$ -D-glucopyranosyl)hexane-2,6-diol;
103. 6-(C- $\beta$ -D-glucopyranosyl)-5-ketopentanoic acid;
104. 6-(C- $\alpha$ -D-glucopyranosyl)-5-ketopentanoic acid;
105. 6-(C- $\beta$ -D-glucopyranosyl)-5-hydroxypentanoic acid;
106. 6-(C- $\alpha$ -D-glucopyranosyl)-5-hydroxypentanoic acid;
107. 6-(C- $\beta$ -D-glucopyranosyl)-5-aminopentanoic acid;
108. 6-(C- $\alpha$ -D-glucopyranosyl)-5-aminopentanoic acid;
109. 6-(C- $\beta$ -D-glucopyranosyl)-5-phenylaminopentanoic acid;



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110. 6-(C- $\alpha$ -D-glucopyranosyl)-5-phenylaminopentanoic acid;
111. 1-(C- $\beta$ -D-glucopyranosyl)pentane-2,5-diol;
112. 1-(C- $\alpha$ -D-glucopyranosyl)pentane-2,5-diol;
113. 1-(C- $\beta$ -D-galactopyranosyl)-2-hydroxypropane;
114. 1-(C- $\alpha$ -D-galactopyranosyl)-2-hydroxypropane;
115. 1-(C- $\beta$ -D-galactopyranosyl)-2-aminopropane;
116. 1-(C- $\alpha$ -D-galactopyranosyl)-2-aminopropane;
117. 1-(C- $\beta$ -D-galactopyranosyl)-2-phenylaminopropane;
118. 1-(C- $\alpha$ -D-galactopyranosyl)-2-phenylaminopropane;
119. ethyl 3-methyl-4-( $\beta$ -D-galactopyranosyl)butyrate;
120. ethyl 3-methyl-4-( $\alpha$ -D-galactopyranosyl)butyrate;
121. 6-(C- $\beta$ -D-galactopyranosyl)-5-ketohexanoic acid;
122. 6-(C- $\alpha$ -D-galactopyranosyl)-5-ketohexanoic acid;
123. 6-(C- $\beta$ -D-galactopyranosyl)-5-hydroxyhexanoic acid;
124. 6-(C- $\alpha$ -D-galactopyranosyl)-5-hydroxyhexanoic acid;
125. 6-(C- $\beta$ -D-galactopyranosyl)-5-aminohexanoic acid;
126. 6-(C- $\alpha$ -D-galactopyranosyl)-5-aminohexanoic acid;
127. 6-(C- $\beta$ -D-galactopyranosyl)-5-phenylaminohexanoic acid;
128. 6-(C- $\alpha$ -D-galactopyranosyl)-5-phenylaminohexanoic acid;
129. 1-(C- $\beta$ -D-galactopyranosyl)hexane-2,6-diol;
130. 1-(C- $\alpha$ -D-galactopyranosyl)hexane-2,6-diol;
131. 6-(C- $\beta$ -D-galactopyranosyl)-5-ketopentanoic acid;
132. 6-(C- $\alpha$ -D-galactopyranosyl)-5-ketopentanoic acid;
133. 6-(C- $\beta$ -D-galactopyranosyl)-5-hydroxypentanoic acid;
134. 6-(C- $\alpha$ -D-galactopyranosyl)-5-hydroxypentanoic acid;
135. 6-(C- $\beta$ -D-galactopyranosyl)-5-aminopentanoic acid;
136. 6-(C- $\alpha$ -D-galactopyranosyl)-5-aminopentanoic acid;
137. 6-(C- $\beta$ -D-galactopyranosyl)-5-phenylaminopentanoic acid;
138. 6-(C- $\alpha$ -D-galactopyranosyl)-5-phenylaminopentanoic acid;
139. 1-(C- $\beta$ -D-galactopyranosyl)pentane-2,6-diol;
140. 1-(C- $\alpha$ -D-galactopyranosyl)pentane-2,6-diol;
141. 1-(C- $\beta$ -D-fucofuranosyl)propan-2-one;
142. 1-(C- $\alpha$ -D-fucofuranosyl)propan-2-one;
143. 1-(C- $\beta$ -L-fucofuranosyl)propan-2-one;
144. 1-(C- $\alpha$ -L-fucofuranosyl)propan-2-one;
145. 3'-(acetamido-C- $\beta$ -D-glucopyranosyl)propane-2'-one;
146. 3'-(acetamido-C- $\alpha$ -D-glucopyranosyl)propane-2'-one;
147. 1-(acetamido-C- $\beta$ -D-glucopyranosyl)-2-hydroxypropane;
148. 1-(acetamido-C- $\beta$ -D-glucopyranosyl)-2-aminopropane;
149. 1-(acetamido-C- $\beta$ -D-glucopyranosyl)-2-phenylaminopropane;
150. 1-(acetamido-C- $\alpha$ -D-glucopyranosyl)-2-phenylaminopropane;
151. ethyl 3-methyl-4-(acetamido-C- $\beta$ -D-glucopyranosyl)butyrate;
152. ethyl 3-methyl-4-(acetamido-C- $\alpha$ -D-glucopyranosyl)butyrate;
153. 6-(acetamido-C- $\beta$ -D-glucopyranosyl)-5-ketohexanoic acid;
154. 6-(acetamido-C- $\alpha$ -D-glucopyranosyl)-5-ketohexanoic acid;
155. 6-(acetamido-C- $\beta$ -D-glucopyranosyl)-5-hydroxyhexanoic acid;
156. 6-(acetamido-C- $\alpha$ -D-glucopyranosyl)-5-hydroxyhexanoic acid;
157. 6-(acetamido-C- $\beta$ -D-glucopyranosyl)-5-aminohexanoic acid;
158. 6-(acetamido-C- $\alpha$ -D-glucopyranosyl)-5-aminohexanoic acid;

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159. 6-(acetamido-C- $\beta$ -D-glucopyranosyl)-5-phenylaminohexanoic acid;
  160. 6-(acetamido-C- $\alpha$ -D-glucopyranosyl)-5-phenylaminohexanoic acid;
  161. 1-(acetamido-C- $\beta$ -D-glucopyranosyl)hexane-2,6-diol;
  162. 1-(acetamido-C- $\alpha$ -D-glucopyranosyl)hexane-2,6-diol;
  163. 6-(acetamido-C- $\beta$ -D-glucopyranosyl)-5-ketopentanoic acid;
  164. 6-(acetamido-C- $\alpha$ -D-glucopyranosyl)-5-ketopentanoic acid;
  165. 6-(acetamido-C- $\beta$ -D-glucopyranosyl)-5-hydroxypentanoic acid;
  166. 6-(acetamido-C- $\alpha$ -D-glucopyranosyl)-5-hydroxypentanoic acid;
  167. 6-(acetamido-C- $\beta$ -D-glucopyranosyl)-5-aminopentanoic acid;
  168. 6-(acetamido-C- $\alpha$ -D-glucopyranosyl)-5-aminopentanoic acid;
  169. 6-(acetamido-C- $\beta$ -D-glucopyranosyl)-5-phenylaminopentanoic acid;
  170. 6-(acetamido-C- $\alpha$ -D-glucopyranosyl)-5-phenylaminopentanoic acid;
  171. 1-(acetamido-C- $\beta$ -D-glucopyranosyl)pentane-2,5-diol;
  172. 1-(acetamido-C- $\alpha$ -D-glucopyranosyl)pentane-2,5-diol.
- As non-limiting illustrations of C-glycoside derivatives that are more particularly suitable for use in the invention, mention may be made especially of the following derivatives:
- C- $\beta$ -D-xylopyranoside-n-propan-2-one,
  - C- $\alpha$ -D-xylopyranoside-n-propan-2-one,
  - C- $\beta$ -D-xylopyranoside-2-hydroxypropane,
  - C- $\alpha$ -D-xylopyranoside-2-hydroxypropane,
  - 1-(C- $\beta$ -D-fucopyranoside)propan-2-one,
  - 1-(C- $\alpha$ -D-fucopyranoside)propan-2-one,
  - 1-(C- $\beta$ -L-fucopyranoside)propan-2-one,
  - 1-(C- $\alpha$ -L-fucopyranoside)propan-2-one,
  - 1-(C- $\beta$ -D-fucopyranoside)-2-hydroxypropane,
  - 1-(C- $\alpha$ -D-fucopyranoside)-2-hydroxypropane,
  - 1-(C- $\beta$ -L-fucopyranoside)-2-hydroxypropane,
  - 1-(C- $\alpha$ -L-fucopyranoside)-2-hydroxypropane,
  - 1-(C- $\beta$ -D-glucopyranosyl)-2-hydroxypropane,
  - 1-(C- $\alpha$ -D-glucopyranosyl)-2-hydroxypropane,
  - 1-(C- $\beta$ -D-galactopyranosyl)-2-hydroxypropane,
  - 1-(C- $\alpha$ -D-galactopyranosyl)-2-hydroxypropane,
  - 1-(C- $\beta$ -D-fucofuranosyl)propan-2-one,
  - 1-(C- $\alpha$ -D-fucofuranosyl)propan-2-one,
  - 1-(C- $\beta$ -L-fucofuranosyl)propan-2-one,
  - 1-(C- $\alpha$ -L-fucofuranosyl)propan-2-one,
  - C- $\beta$ -D-maltopyranoside-n-propan-2-one,
  - C- $\alpha$ -D-maltopyranoside-n-propan-2-one,
  - C- $\beta$ -D-maltopyranoside-2-hydroxypropane,
  - C- $\alpha$ -D-maltopyranoside-2-hydroxypropane, isomers thereof and mixtures thereof.

According to one embodiment, C- $\beta$ -D-xylopyranoside-2-hydroxypropane or C- $\alpha$ -D-xylopyranoside-2-hydroxypropane, and better still C- $\beta$ -D-xylopyranoside-2-hydroxypropane, may advantageously be used for the preparation of a composition according to the invention.

According to one particular embodiment, the C-glycoside derivative may be C- $\alpha$ -D-xylopyranoside-2-hydroxypropane in the form of a solution containing 30% of active material in a water/propylene glycol mixture (60%/40% by weight), such as the product manufactured by Chimex under the trade name Mexoryl SDB®.

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Needless to say, according to the invention, a C-glycoside derivative corresponding to formula (I) may be used alone or as a mixture with other C-glycoside derivatives and in all proportions.

A C-glycoside derivative that is suitable for use in the invention may especially be obtained via the synthetic method described in document WO 02/051 828.

The amount of C-glycoside derivative to be used in a composition according to the invention depends on the desired cosmetic or therapeutic effect, and may thus vary within a wide range.

A person skilled in the art can readily determine the appropriate amounts, on the basis of his general knowledge.

A composition in accordance with the invention may comprise a C-glycoside derivative in a proportion of about from 0.0001% to about 25% by weight relative to the total weight of the composition, and in particular from about 0.001% to about 10% by weight and even more particularly between 0.05% and 5% by weight of C-glycoside derivative active material relative to the total weight of the composition.

#### Additives

The C-glycoside derivative(s) may be used in combination with other active agents.

Typically, according to one aspect of the invention, the C-glycoside derivative(s) may be used in combination with at least:

- one moisturizing product,
- one epidermal or dermal protease effector,
- one enzyme and especially one exogenous protease and/or glycosidase and/or lipase, and/or
- one active agent for improving epidermal differentiation, and/or
- one anti-seborrhoeic agent.

The term "moisturizer" means;

either a compound that acts on the barrier function, in order to maintain the moisturization of the stratum corneum, or an occlusive compound. Mention may be made of ceramides, sphingoid-based compounds, lecithins, glycosphingolipids, phospholipids, cholesterol and derivatives thereof, phytosterols (stigmasterol,  $\beta$ -sitosterol or campesterol), essential fatty acids, 1,2-diacylglycerol, 4-chromanone, pentacyclic triterpenes such as ursolic acid, petroleum jelly and lanolin;

or a compound that directly increases the water content of the stratum corneum, such as trehalose and derivatives thereof, hyaluronic acid and derivatives thereof, glycerol, pentanediol, sodium pidolate, serine, xylitol, sodium lactate, polyglyceryl acrylate, ectoin and derivatives thereof, chitosan, oligosaccharides and polysaccharides, cyclic carbonates, N-lauroylpyrrolidonecarboxylic acid and N- $\alpha$ -benzoyl-L-arginine;

or a compound that activates the sebaceous glands, such as steroid derivatives (including DHEA) and vitamin D and derivatives thereof. This latter category of compounds will be more particularly suitable for application to mature skin, or even very mature skin, for example in the case of individuals more than 55 or 60 years old.

A urea derivative described especially in patent application DE-A-2 703 185 may especially be incorporated into the composition. Among these, N-(2-hydroxyethyl)urea is also commercially available, in the form of a mixture at 50% by weight in water, from the company National Starch under the trade name Hydrovance®.

These compounds may represent from 0.001% to 20% and preferably from 0.01% to 10% of the total weight of the composition according to the invention, and even more

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preferentially between 0.05% and 5% by weight relative to the total weight of the composition.

The use of at least one C-glycoside derivative in combination with at least one moisturizer mentioned above is advantageously intended for preventing or treating xerosis.

The expression "epidermal or dermal protease effector" means any molecule capable of inhibiting or activating enzymes via direct interactions (e.g.: protease inhibitors) or via indirect interactions with the substrates (e.g.: urea and urea derivatives), but also molecules capable of modulating the microenvironment of the enzyme (presence of effector salts, pH changes, etc.).

The term "effector" covers the possible use of protease inhibitors when certain activities are undesirable, such as the inhibitors of certain serine proteases (such as urokinase, chymotrypsins or trypsin) and metalloproteases. Specifically, it is known that certain enzymes have a deleterious effect on the constituents of the dermis or of the epidermis and their activity should be suppressed in order to obtain an optimum effect on the aspect and radiance of the skin.

The compositions according to the invention may also contain other enzymes and in particular exogenous proteases, and/or glycosidases and/or lipases and/or amidases. Such compounds are conventionally used in desquamating compositions and/or compositions for accelerating the renewal of the horny layer, and the combination of at least one C-glycoside compound as defined above will make it possible to reinforce and/or prolong their action.

The expression "exogenous proteases and/or glycosidases and/or lipases" means enzymes of recombinant origin or enzymes present in plant extracts, such as serine proteases, aspartic acid proteases, cysteine proteases or metalloproteases, glycosidases belonging to the family of exoglycosidases or endoglycosidases, and acidic or basic lipases.

The concentrations of these enzymes will be adapted according to the degree of purity and the activity of the product containing them. They are generally from 0.0001% to 5%, but may be lowered to concentrations of less than or equal to 1%, or even less than or equal to 0.1%, in combination with compounds of formula (I) according to the invention.

The term "active agent for improving epidermal differentiation" means an active agent capable of promoting and/or accelerating epidermal stratification resulting in a barrier function of better quality and/or an epidermal aspect of yellow skin type, especially with combating of the flattening of the dermo-epidermal junction.

Among these active agents, mention may be made of 8-hexadecene-1,16-dicarboxylic acid (dioic acid), vitamin D derivatives, ecdysterone and PPAR agonists, active agents for promoting the synthesis of epidermal glycosaminoglycans and proteoglycans such as Perlecan, histone deacetylase inhibitors, and growth factors or analogues thereof such as KGF or LIF.

The compositions according to the invention may also contain anti-seborrhoeic agents and, for example, a 5- $\alpha$ -reductase inhibitor; these agents may be chosen especially from:

- retinoids, and in particular retinol;
- sulfur and sulfur derivatives;
- zinc salts such as zinc lactate, gluconate, pidolate, carboxylate, salicylate and/or cysteate;
- selenium chloride;
- vitamin 86 or pyridoxine;
- the mixture of capryloyl glycine, sarcosine and extract of *Cinnamomum zeylanicum* sold especially by the company SEPPIC under the trade name Sepicontrol A5®;

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an extract of *Laminaria saccharina* sold especially by the company Biotech Marine under the trade name Phlorogine®;

an extract of *Spiraea ulmaria* sold especially by the company Silab under the trade name Sebonormine®;

plant extracts from the species *Arnica montana*, *Cinchona succirubra*, *Eugenia caryophyllata*, *Humulus lupulus*, *Hypericum perforatum*, *Mentha piperita*, *Rosmarinus officinalis*, *Salvia officinalis* and *Thymus vulgaris*, all sold, for example, by the company Maruzen;

an extract of *Serenoa repens* sold especially by the company Euromed;

plant extracts of the genus *Silybum*; and

extracts of *Eugenia caryophyllata* containing eugenol and eugenyl glucoside.

The compositions containing such agents will be more particularly intended for treating greasy or hyperseborrhoeic skin.

A composition according to the invention may be for cosmetic and/or pharmaceutical use, and especially for dermatological use.

The compositions according to the invention comprise a physiologically acceptable vehicle, i.e. a medium that is compatible with any keratin material such as the skin, the scalp, the nails, mucous membranes, the eyes and the hair. According to one preferred embodiment of the invention, the composition has a pH close to that of the skin, of between 4 and 7.

The physiologically acceptable medium may comprise an aqueous phase, optionally as a mixture with one or more organic solvents such as a C<sub>1</sub>-C<sub>8</sub> alcohol, especially ethanol, isopropanol, tert-butanol, n-butanol, polyols, for instance glycerol, propylene glycol, butylene glycol, and polyol ethers. It may also be anhydrous.

A composition according to the invention may also comprise a fatty phase, which may comprise oils, gums or waxes usually used in the field of application under consideration.

When the composition of the invention is an emulsion, the proportion of the fatty phase may range from 5% at 80% by weight and preferably from 5% to 50% by weight relative to the total weight of the composition.

The oils, waxes, emulsifiers and coemulsifiers used in the composition in emulsion form are chosen from those conventionally used in the field under consideration. The emulsifier and the coemulsifier are generally present in the composition in a proportion ranging from 0.3% to 30% by weight and preferably from 0.5% to 20% by weight relative to the total weight of the composition. The emulsion may also contain lipid vesicles.

As oils that may be used in the composition of the invention, examples that may be mentioned include:

hydrocarbon-based oils of animal origin, such as perhydro-squalene;

hydrocarbon-based oils of plant origin, such as liquid triglycerides of fatty acids containing from 4 to 10 carbon atoms and the liquid fraction of shea butter;

synthetic esters and synthetic ethers, especially of fatty acids, for instance oils of formulae R<sub>1</sub>COOR<sub>2</sub>, and R<sub>1</sub>OR<sub>2</sub> in which R<sub>1</sub> represents a fatty acid residue containing from 8 to 29 carbon atoms and R<sub>2</sub> represents a branched or unbranched hydrocarbon-based chain containing from 3 to 30 carbon atoms, such as, for example, purcellin oil, isononyl isononanoate, isopropyl myristate, 2-ethylhexyl palmitate, 2-octyldodecyl stearate, 2-octyldodecyl erucate, isostearyl isostearate; hydroxylated esters such as isostearyl lactate, octyl hydroxystearate, octyldodecyl hydroxystearate, diisostearyl malate, triisocetyl citrate and fatty alkyl

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heptanoates, octanoates and decanoates; polyol esters, for instance propylene glycol dioctanoate, neopentyl glycol diheptanoate and diethylene glycol diisononanoate; and pentaerythritol esters, for instance pentaerythrityl tetraistearate;

linear or branched hydrocarbons of mineral or synthetic origin, such as volatile or non-volatile liquid paraffins, and derivatives thereof, petroleum jelly, polydecenes, and hydrogenated polyisobutene such as parleam oil;

fatty alcohols containing from 8 to 26 carbon atoms, for instance cetyl alcohol, stearyl alcohol and a mixture thereof (cetylstearyl alcohol), octyldodecanol, 2-butyloctanol, 2-hexyldecanol, 2-undecylpentadecanol, oleyl alcohol or linoleyl alcohol;

partially hydrocarbon-based and/or silicone-based fluoro oils, for instance those described in document JP-A-2 295 912;

silicone oils, for instance volatile or non-volatile polymethylsiloxanes (PDMSs) containing a linear or cyclic silicone chain, that are liquid or pasty at room temperature, especially cyclopolydimethylsiloxanes (cyclomethicones) such as cyclohexasiloxane; polydimethylsiloxanes comprising alkyl, alkoxy or phenyl groups, which are pendent or at the end of a silicone chain, these groups containing from 2 to 24 carbon atoms; phenyl silicones, for instance phenyl trimethicones, phenyl dimethicones, phenyltrimethylsiloxy-diphenylsiloxanes, diphenyl dimethicones, diphenylmethyl-diphenyltrisiloxanes, 2-phenylethyltrimethyl siloxysilicates and polymethylphenylsiloxanes; and

mixtures thereof.

As emulsifiers and coemulsifiers that may be used in the invention, examples that may be mentioned include O/W emulsifiers such as fatty acid esters of polyethylene glycol, especially PEG-100 stearate, and fatty acid esters of glycerol such as glyceryl stearate, and also W/O emulsifiers such as the oxyethylenated poly(methylcetyl)(dimethyl)methylsiloxane sold under the trade name Abil WE 09 by the company Degussa-Goldschmidt.

In a known manner, the composition according to the invention may also contain adjuvants that are common in cosmetics and dermatology, such as hydrophilic or lipophilic gelling agents, preserving agents, antioxidants, solvents, fragrances, fillers, screening agents, pigments, odour absorbers and dyestuffs. The amounts of these various adjuvants are those conventionally used in the field under consideration, for example from 0.01% to 20% of the total weight of the composition. Depending on their nature, these adjuvants may be introduced into the fatty phase, into the aqueous phase and/or into lipid spherules. In any case, these adjuvants, and the proportions thereof, will be chosen so as not to harm the properties desired for the compound according to the invention.

Hydrophilic gelling agents that may be mentioned in particular include carboxyvinyl polymers (carbomer), acrylic copolymers such as acrylate/alkylacrylate copolymers, polyacrylamides, polysaccharides, natural gums and clays, and lipophilic gelling agents that may be mentioned include modified clays, for instance bentonites, metal salts of fatty acids, hydrophobic silica and polyethylenes.

As fillers that may be used in the composition of the invention, besides pigments, examples that may be mentioned include silica powder; talc; starch crosslinked with octenylsuccinic anhydride, sold by the company National Starch under the name Dry-Flo Plus (28-1160); polyamide particles and especially those sold under the name Orgasol by the company Atochem; polyethylene powders; microspheres based on acrylic copolymers, such as those made of

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ethylene glycol dimethacrylate/lauryl methacrylate copolymer sold by the company Dow Corning under the name Polytrap; expanded powders such as hollow microspheres, and especially the microspheres sold under the name Expancel by the company Kemanord Plast or under the name Micropearl F 80 ED by the company Matsumoto; silicone resin microbeads such as those sold under the name Tospearl by the company Toshiba Silicone; and mixtures thereof. These fillers may be present in amounts ranging from 0 to 20% by weight and preferably from 1% to 10% by weight relative to the total weight of the composition according to the invention.

The compositions that may be used according to the invention may be ingested, injected or applied to the skin (to any area of bodily skin), the hair, the nails or mucous membranes (oral, jugal, gingival, genital or connective tissue membranes).

According to the adopted mode of administration, a composition according to the invention may be in any galenical form normally used, particularly in cosmetology. For obvious reasons, the amount of C-glycoside in the compositions according to the invention is liable to vary significantly as a function of the intended purpose of the composition and/or of its mode of administration.

In general, the C-glycoside derivative may be used in topical mode at a concentration of between 0.01% and 25% by weight and preferably between 0.5% and 20% by weight of active material relative to the total weight of the composition.

The compositions according to the invention are preferably formulated in a form that is suitable for topical administration.

When it is applied topically, the composition comprising at least one C-glycoside derivative may be applied to the face, the neck, the scalp, mucous membranes and the nails or to any other area of bodily skin.

The application times will vary as a function of the concentration of C-glycoside in the composition, and of the desired effect. As a guide, the composition may remain in contact with the skin or the integuments for between 5 minutes and 12 hours, and may optionally be removed after this contact time. The application may be performed daily or twice-daily, or weekly, and repeated for periods of 2 weeks to 6 months; this period may be prolonged or renewed without difficulty.

These compositions are especially in the form of aqueous, aqueous-alcoholic or oily solutions, dispersions of the lotion or serum type, anhydrous or oily gels, emulsions of liquid or semi-liquid consistency of the milk type, obtained by dispersing a fatty phase in an aqueous phase (O/W) or conversely (W/O), suspensions or emulsions of soft, semi-solid or solid consistency of the cream or gel type, microemulsions, or alternatively microcapsules, microparticles or vesicular dispersions of ionic and/or nonionic type. These compositions are prepared according to the usual methods.

The amounts of the various constituents of the compositions used according to the invention are those conventionally used in the fields under consideration.

These compositions especially constitute protective, treating or care creams for the face, the hands or the body, protective or care body milks, lotions, gels or mousses for caring for the skin and mucous membranes or for cleansing the skin, masks or patches.

The compositions may also consist of solid preparations constituting cleansing soaps or bars.

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The compositions that may be used according to the invention may also be packaged in the form of an aerosol composition also comprising a pressurized propellant.

During topical application, the composition may be applied directly to the damaged area or to its vicinity, or alternatively, in the case of pathologies comprising crisis periods and rest periods, at a site bearing a lesion, as a preventive measure, to prolong a state of remission between two crises.

Thus, the invention also relates to the use of at least one C-glycoside derivative for the preparation of a composition for treating skin showing signs of deregulation of desquamation.

The compositions according to the invention are especially exfoliant compositions suitable for scrubbing rough areas from the skin. They may also be peeling compositions, for removing a larger thickness of horny layer such as corns.

Compositions according to the invention are also compositions intended for cleansing the skin and/or the scalp, in which the action of the cleansing agents will be reinforced by promoting the removal of dead cells from the cleansed surface.

According to yet another aspect of the invention, the composition containing the compound of formula (I) or derivatives thereof is a care composition for improving the surface condition of the skin and/or mucous membranes, especially the lips; in particular, the said composition will promote the removal of rough areas and/or dead skin present at the surface of the skin and/or the lips.

According to another embodiment of the invention, the compositions are intended for promoting cicatrization, by promoting the removal of adhesions.

The composition that may be used according to the invention may also be a haircare composition, especially a shampoo, a hairsetting lotion, a medicated lotion, a styling cream or gel, a dye composition (especially for oxidation dyeing) optionally in the form of colouring shampoos, restructuring lotions for the hair, a permanent-waving composition (especially a composition for the first stage of a permanent-waving operation), a composition for inducing and/or stabilizing natural hair loss in man, advantageously a lotion or gel, an antiparasitic shampoo, etc.

The invention is illustrated in greater detail in the examples that follow. These examples shall not in any way limit the scope of the invention.

## EXAMPLE

### Characterization of the Desquamating Activity of a C-Glycoside

The C-glycoside derivative used in the examples below is C- $\beta$ -D-xylopyranoside-n-propane-2-one sold under the name Mexoryl SBB® by Chimex. It is in the form of a solution at 30% by weight of active material (AM) in a 60/40 water/1,2-propanediol mixture.

#### Principle of the Test:

In this test, corneodesmosine is sought by immunodetection after incubation. Corneodesmosine is one of the key markers of desquamation of corneodesmosines. It is studied on an immunoblot after electrophoresis separation and transfer onto a membrane. After specific labelling with the antibody G3619, it is revealed by chemiluminescence.

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Materials and Methods:  
Formulae Studied:

Formula	Formula	5
Excipient (Arlacel/Myrj base)	1	
C- $\beta$ -D-xylopyranoside-2-hydroxypropane	2	
Glycerol	3	

Chemical Name	% by weight		
	1	2	3
C- $\beta$ -D-xylopyranoside-2-hydroxypropane (AM)	—	7	—
Triethanolamine	0.3	0.3	0.3
Propyl p-hydroxybenzoate	0.1	0.1	0.1
Methyl p-hydroxybenzoate	0.2	0.2	0.2
Cetyl alcohol	1	1	1
Stearyl alcohol	1	1	1
Hydrogenated isoparaffin (6-8 mol of isobutylene) (Parleam sold by NoF Corporation)	5	5	5
Carboxyvinyl polymer synthesized in an ethyl acetate/cyclohexane mixture (Carbopol 981, sold by Noveon)	0.3	0.3	0.3
Cyclopentadimethylsiloxane	15	15	15
Deionized water	qs 100	qs 100	qs 100
Glycerol	—	—	7
Polyethylene (50 EO) glycol monostearate (Myrj 53P sold by Uniqema)	2.5	2.5	2.5
Glyceryl mono/distearate/polyethylene glycol (100 EO) stearate mixture (Arlacel 165 FL sold by Uniqema)	2.5	2.5	2.5

AM: active material

#### Test Protocol:

3×3.5 cm rectangles are cut out of varnish strippings performed on the calf area of legs bearing dry skin. They are each treated with 42 mg of product (4 mg/cm<sup>2</sup>). Controls and tests are performed in parallel. A blank without product is prepared under the same conditions.

The tests are incubated at 37° C. and 70% relative humidity for 5 days. The controls are stored for 5 days at -20° C. Thus, 5 tests and 5 controls are obtained.

For each of the samples, acetone powders are prepared and weighed out. The proteins are extracted with 100  $\mu$ l/mg of whole Laemmli buffer. They are assayed according to the Bradford method. The protein content of each sample is adjusted and allows a direct comparison of the various samples. The proteins are separated by SDS-Page electrophoresis on 12% acrylamide gel.

After transferring the proteins onto a PVDF membrane, the immunodetection is performed with the anticorneodesmosine antibody G3619 (Guy Serre) at 1/12500 according to a standard western blot technique. Revelation is performed by chemiluminescence. The bands detected by the Fluor Smax machine (Biorad) are quantified with the quantity-one software (Biorad).

#### Results:

The results represent the quantification of the corneodesmosines.

Quantification of the corneodesmosine bands for each sample units: cnt\*mm<sup>2</sup>

	Corneodesmosines	
	Control	Test
Formula 1	2198	2690
Formula 2	2229	1192

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-continued

	Corneodesmosines	
	Control	Test
Formula 3	2748	904
Blank	1667	1710

The table below shows the percentage of residual corneodesmosines of the test relative to the control. The lower the percentage, the more the corneodesmosine is degraded.

% of residual corneodesmosines	
Formula 1	122
Formula 2	53
Formula 3	33
Blank	103

The blank represents the “self-hydrolysis” of the corneodesmosine under the operating conditions of the test. No degradation of the corneodesmosine is observed for the blank.

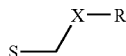
The excipient (Arlacel/Myrj base) is a neutral support close to the blank without treatment.

Glycerol, which is the positive blank, shows substantial degradation of corneodesmosine. The C- $\beta$ -D-xylopyranoside-2-hydroxypropane tested shows a positive effect in this test.

The invention claimed is:

1. A cosmetic method for promoting desquamation of the skin and/or the scalp comprising at least the topical administration to the skin and/or the scalp, as a cosmetic agent, of at least one C-glycoside derivative in a composition comprising a physiologically acceptable medium to promote desquamation to thereby treat xerosis, acne, hyperkeratosis, or ichthyosis, wherein the C-glycoside derivative corresponds to the general formula (I) below:

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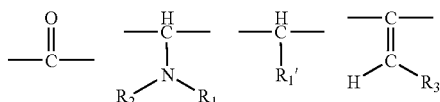
in which:

R represents:

a linear C<sub>1</sub>-C<sub>4</sub> radical, optionally substituted with —OH, —COOH or —COOR''<sub>2</sub>,

R''<sub>2</sub> being a saturated C<sub>1</sub>-C<sub>4</sub> alkyl radical;

X represents a radical chosen from the groups:



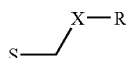
with R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> representing, independently of each other, a hydrogen atom or a radical R, with R as defined above, and R<sub>1</sub>' represents a hydrogen atom, an —OH group or a radical R as defined above, R<sub>1</sub> can also be a C<sub>6</sub>-C<sub>10</sub> aryl radical;

S represents a monosaccharide or a polysaccharide comprising up to 20 sugar units, in pyranose and/or furanose form and of L and/or D series, the mono- or polysaccharide optionally being substituted with a mandatorily free hydroxyl group or one or more protected amine function(s), and

the bond S—CH<sub>2</sub>—X represents a bond of C-anomeric nature, which is α or β,

and also the cosmetically acceptable salts thereof, the solvates thereof and the isomers thereof, the C-glycoside derivative being present in a proportion of 0.05% to 10% by weight relative to the total weight of the composition.

2. A method for treating signs associated with a desquamation disorder comprising the topical administration to the skin and/or the scalp of at least one C-glycoside derivative to treat the signs associated with the desquamation disorder, wherein the desquamation disorder is selected from the group consisting of xerosis, acne, hyperkeratosis, and ichthyosis, and the C-glycoside derivative corresponds to the general formula (I) below:



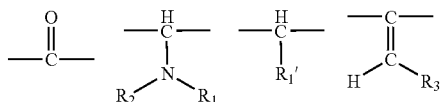
in which:

R represents:

a linear C<sub>1</sub>-C<sub>4</sub> radical, optionally substituted with —OH, —COOH or —COOR''<sub>2</sub>,

R''<sub>2</sub> being a saturated C<sub>1</sub>-C<sub>4</sub> alkyl radical;

X represents a radical chosen from the groups:



with R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> representing, independently of each other, a hydrogen atom or a radical R, with R as

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defined above, and R<sub>1</sub>' represents a hydrogen atom, an —OH group or a radical R as defined above, R<sub>1</sub> can also be a C<sub>6</sub>-C<sub>10</sub> aryl radical;

S represents a monosaccharide or a polysaccharide comprising up to 20 sugar units, in pyranose and/or furanose form and of L and/or D series, the mono- or polysaccharide optionally being substituted with a mandatorily free hydroxyl group or one or more protected amine function(s), and

the bond S—CH<sub>2</sub>—X represents a bond of C-anomeric nature, which is α or β,

and also the cosmetically acceptable salts thereof, the solvates thereof and the isomers thereof.

3. The method according to claim 1, in which S represents a monosaccharide chosen from D-glucose, D-xylose, L-fucose, D-galactose and D-maltose.

4. The method according to claim 1, in which X represents a group chosen from —CO—, —CH(OH)— and —CH(NH<sub>2</sub>)—.

5. The method according to claim 1, in which the C-glycoside derivative is chosen from:

C-β-D-xylopyranoside-n-propan-2-one,  
C-α-D-xylopyranoside-n-propan-2-one,  
C-β-D-xylopyranoside-2-hydroxypropane,  
C-α-D-xylopyranoside-2-hydroxypropane,  
1-(C-β-D-fucopyranoside)propan-2-one,  
1-(C-α-D-fucopyranoside)propan-2-one,  
1-(C-β-L-fucopyranoside)propan-2-one,  
1-(C-α-L-fucopyranoside)propan-2-one,  
1-(C-β-D-fucopyranoside)-2-hydroxypropane,  
1-(C-α-D-fucopyranoside)-2-hydroxypropane,  
1-(C-β-L-fucopyranoside)-2-hydroxypropane,  
1-(C-α-L-fucopyranoside)-2-hydroxypropane,  
1-(C-β-D-glucopyranosyl)-2-hydroxypropane,  
1-(C-α-D-glucopyranosyl)-2-hydroxypropane,  
1-(C-β-D-galactopyranosyl)-2-hydroxypropane,  
1-(C-α-D-galactopyranosyl)-2-hydroxypropane,  
1-(C-β-D-fucofuranosyl)propan-2-one,  
1-(C-α-D-fucofuranosyl)propan-2-one,  
1-(C-β-L-fucofuranosyl)propan-2-one,  
1-(C-α-L-fucofuranosyl)propan-2-one,  
C-β-D-maltopyranoside-n-propan-2-one,  
C-α-D-maltopyranoside-n-propan-2-one,  
C-β-D-maltopyranoside-2-hydroxypropane,  
C-α-D-maltopyranoside-2-hydroxypropane, isomers thereof and mixtures thereof.

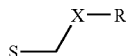
6. The method according to claim 1 in which the C-glycoside derivative is chosen from C-β-D-xylopyranoside-2-hydroxypropane and C-α-D-xylopyranoside-2-hydroxypropane.

7. The method according to claim 1, in which the C-glycoside derivative is used in combination with at least:

one moisturizing product,  
one epidermal or dermal protease effector,  
one exogenous protease and/or glycosidase and/or lipase,  
one active agent for improving epidermal differentiation, and/or  
one anti-seborrhoeic agent.

8. A cosmetic treatment process for promoting desquamation, comprising at least the topical administration to the skin and/or the scalp of a composition comprising, in a physiologically acceptable medium, at least one C-glycoside derivative to promote desquamation to thereby treat xerosis, acne, hyperkeratosis, or ichthyosis, wherein the C-glycoside derivative corresponds to the general formula (I) below:

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(I)

in which:

R represents:

a saturated C<sub>1</sub>-C<sub>20</sub> or unsaturated C<sub>2</sub>-C<sub>20</sub> linear alkyl radical, or a saturated or unsaturated, branched or cyclic C<sub>3</sub>-C<sub>20</sub> alkyl radical;

a saturated C<sub>1</sub>-C<sub>20</sub> or unsaturated C<sub>2</sub>-C<sub>20</sub> linear, or saturated or unsaturated, branched or cyclic C<sub>3</sub>-C<sub>20</sub> hydrofluoroalkyl or perfluoroalkyl radical;

the hydrocarbon-based chain constituting the radicals optionally being, where appropriate, interrupted with 1, 2, 3 or more heteroatoms chosen from:

an oxygen,

a sulfur,

a nitrogen, and

a silicon,

and being optionally substituted with at least one radical chosen from:

—OR<sub>4</sub>,

—SR<sub>4</sub>,

—NR<sub>4</sub>R<sub>5</sub>,

—COOR<sub>4</sub>,

—CONHR<sub>4</sub>,

—CN,

a halogen atom,

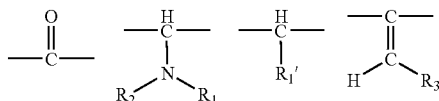
a C<sub>1</sub>-C<sub>6</sub> hydrofluoroalkyl or perfluoroalkyl radical, and/or

a C<sub>3</sub>-C<sub>8</sub> cycloalkyl radical,

with R<sub>4</sub> and R<sub>5</sub> representing, independently of each other, a hydrogen atom or a saturated C<sub>1</sub>-C<sub>30</sub> or unsaturated C<sub>2</sub>-C<sub>30</sub> linear, or a saturated or unsaturated, branched or cyclic C<sub>3</sub>-C<sub>30</sub> alkyl, perfluoroalkyl or hydrofluoroalkyl radical;

or a C<sub>6</sub>-C<sub>10</sub> aryl radical;

X represents a radical chosen from the groups:



with R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> representing, independently of each other, a hydrogen atom or a radical R, with R as defined above, and R<sub>1</sub>' represents a hydrogen atom, an —OH group or a radical R as defined above, R<sub>1</sub> can also be a C<sub>6</sub>-C<sub>10</sub> aryl radical;

S represents a monosaccharide or a polysaccharide comprising up to 20 sugar units, in pyranose and/or furanose form and of L and/or D series, the mono- or polysaccharide optionally being substituted with a

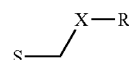
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mandatorily free hydroxyl group or one or more protected amine function(s), and

the bond S—CH<sub>2</sub>—X represents a bond of C-anomeric nature, which is α or β,

and also the cosmetically acceptable salts thereof, the solvates thereof and the isomers thereof, the C-glycoside derivative being present in a proportion of 0.05% to 10% by weight relative to the total weight of the composition.

9. A method to promote regular desquamation of reconstructed skin comprising at least the topical administration to the reconstructed skin of a composition comprising, in a physiologically acceptable medium, at least one C-glycoside derivative to promote regular desquamation of the reconstructed skin, wherein the C-glycoside derivative corresponds to the general formula (I) below:



(I)

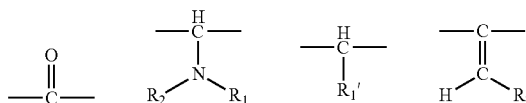
in which:

R represents:

a linear C<sub>1</sub>-C<sub>4</sub> radical, optionally substituted with —OH, —COOH or —COOR<sub>2</sub>,

R<sub>2</sub> being a saturated C<sub>1</sub>-C<sub>4</sub> alkyl radical;

X represents a radical chosen from the groups:



with R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> representing, independently of each other, a hydrogen atom or a radical R, with R as defined above, and R<sub>1</sub>' represents a hydrogen atom, an —OH group or a radical R as defined above, R<sub>1</sub> can also be a C<sub>6</sub>-C<sub>10</sub> aryl radical;

S represents a monosaccharide or a polysaccharide comprising up to 20 sugar units, in pyranose and/or furanose form and of L and/or D series, the mono- or polysaccharide optionally being substituted with a mandatorily free hydroxyl group or one or more protected amine function(s), and

the bond S—CH<sub>2</sub>—X represents a bond of C-anomeric nature, which is α or β, and also the cosmetically acceptable salts thereof, the solvates thereof and the isomers thereof, the C-glycoside derivative being present in a proportion of 0.05% to 10% by weight relative to the total weight of the composition.

\* \* \* \* \*